

IN THE CLAIMS:

The below listing of claims will replace all prior versions and listings of claims in the application.

1. (canceled)
2. (currently amended) A recombinant vector ~~derived from an~~ based on a native adenovirus comprising at least one ITR and a packaging signal, the recombinant vector having a first insertion site for a nucleic acid sequence of interest, a second insertion site for ~~functionally~~ inserting a gene sequence encoding at least a part of a penton and/or hexon protein of a first adenovirus serotype, and a third insertion site for a gene sequence encoding a part of a fiber protein of a second adenovirus serotype, the second adenovirus serotype selected from the group consisting of serotypes 11, 14, 16, 21, 34, 35, and 50, a gene sequence encoding at least a part of a penton and/or hexon protein from the first adenovirus serotype inserted into the second insertion site, a gene sequence encoding the part of a fiber protein of the second adenovirus serotype inserted into the third insertion site, the gene sequence encoding the part of a fiber protein adapted to exhibit a desired tropism to a plurality of target cells in a host and fused to a tail region of a fiber of the native adenovirus serotype ~~from which the recombinant vector was derived~~.

3. (previously presented) The recombinant vector of claim 2 wherein the recombinant vector comprises a plasmid.

4.-12. (canceled)

13. (withdrawn) A method for selecting and producing a chimeric adenovirus having a desired host range determined by at least one part of a fiber of a first adenovirus serotype and immunological properties determined by at least one part of at least one of a hexon or a penton of a second adenovirus serotype, said method comprising:

providing a recombinant vector derived from an adenovirus comprising at least one ITR and a packaging signal, said recombinant vector having an insertion site for a gene of interest, said recombinant vector further having an insertion site for a nucleic acid encoding at least one part of a fiber protein of the first adenovirus subtype and having an insertion site for functionally inserting a nucleic acid encoding at least one part of at least one of a penton or a hexon protein of the second adenovirus subtype;

providing a nucleic acid library comprising a plurality of nucleic acids encoding a plurality of adenoviral protein of a plurality of adenovirus serotypes, said plurality of nucleic acids flanked by restriction sites wherein said restriction sites correspond to said insertion sites in said recombinant vector;

inserting into said recombinant vector at least one first nucleic acid from said nucleic acid library,

said at least one first nucleic acid obtained from the second adenovirus serotype and encoding at least one parrot of at least one of a penton or hexon proteins of the first adenovirus serotype and conferring a viral particle having lower antigenicity;
inserting into said recombinant vector at least one second nucleic acid from said nucleic acid library, said at least one second nucleic acid obtained from the first adenovirus serotype and encoding at least on functional part of a fiber protein having the desired host range;
providing at least one packaging cell;
transfecting said recombinant vector into said at least one packaging cell; and
producing chimeric virus particles.

14. (withdrawn) The method according to claim 13, further comprising inserting said gene of interest into said recombinant vector prior to said transfecting.

15. (withdrawn) The method according to claim 14, wherein said providing a recombinant vector comprises providing an expression cassette for said gene of interest.

16. (withdrawn) The method according to claim 1, wherein said providing a nucleic acid library comprises providing a plurality of nucleic acids encoding proteins of like functions for differing adenovirus serotypes, and wherein said plurality of nucleic acids encoding proteins of like functions for differing adenovirus serotypes are flanked by uniform restriction sites.

17. (withdrawn) The method according to claim 13, wherein said providing a recombinant vector comprises providing a vector lacking the E1 adenoviral genome.

18. (withdrawn) The method according to claim 17, wherein said providing at least one packaging cell comprises providing at least one packaging cell selected from the group consisting of PER.C6, 911, 293, and E1 A549 cells.

19. (withdrawn) The method according to claim 13, wherein said providing a recombinant vector derived from an adenovirus Sub-Group C serotype

20. (withdrawn) The method according to claim 19, wherein said adenovirus Sub-Group C serotype comprises one of Ad2 or Ad5.

21. (withdrawn) The method according to claim 13, wherein said at least one first nucleic acid is obtained from an adenovirus Sub-Group B or C serotype.

22. (withdrawn) The method according to claim 13, wherein said at least one second nucleic acid is obtained from an adenovirus Sub-Group B or C serotype.

23. (withdrawn) The method according to claim 13, wherein said providing a recombinant vector comprises providing a vector selected from the group consisting of viral, plasmid, and cosmid vectors.

24. (withdrawn) The method according to claim 13, wherein said at least one second nucleic acid obtained from the first adenovirus serotype comprises a nucleic acid encoding a knob protein of a fiber protein, and wherein said at least one first nucleic acid obtained from a second adenovirus serotypes further comprises a nucleic acid encoding a base protein of a fiber protein and a shaft protein of a fiber protein.

25. (withdrawn) The method according to claim 13, wherein said providing a nucleic acid library comprises providing nucleic acids carrying sequence mutations, and wherein said nucleic acids carrying sequence mutations encode proteins screened for characteristics selected from the group consisting of temperature stability, assembly, anchoring, redirected infection, and altered immune response.

26. (withdrawn) The method according to claim 13, wherein said providing a nucleic acid library comprises providing nucleic acids encoding a plurality of adenoviral proteins obtained from a plurality of adenovirus serotypes selected from the group consisting of adenovirus Sub-Groups A, B, C, D, E, F, G.

27. (withdrawn) A library of chimeric adenovirus produced by the method according to claim 13.

28. (withdrawn) A method of generating a library of chimeric adenoviruses, said method comprising:

providing a plurality of recombinant vectors derived from an adenoviral genome, each of said

plurality of recombinant vectors having an insertion site for a nucleic acid encoding at least on part of a fiber protein of an adenovirus subtype having a desired host range and having an insertion site for functionally inserting a nucleic acid encoding at least one part of at least one of a penton or a hexon protein of a different adenovirus serotype having predetermined antigenic properties;

providing a nucleic acid library comprising a plurality of nucleic acids encoding a plurality of adenoviral proteins of a plurality of adenovirus serotypes, said plurality of nucleic acids flanked by restriction sites wherein said restriction sites correspond to said insertion sites in said recombinant vector;

inserting into each of said plurality of recombinant vectors at least one first nucleic acid from said nucleic acid library encoding at least one functional part of a fiber protein obtained from a adenovirus serotype having a desired host range;

inserting into each of said plurality of recombinant vectors at least one second nucleic acid from

said nucleic acid library encoding at least one functional part of a penton or hexon protein of different adenovirus serotype having predetermined antigenic properties, said penton or hexon protein of each respective recombinant vector having lower antigenicity relative to penton or hexon proteins of the adenovirus serotype conferring the desired host range and resulting in a viral particle having lower antigenicity;

providing a plurality of packaging cells;

transfecting said plurality of recombinant vectors into said plurality of packaging cells; and

producing a library of chimeric viral particles defined by differing fiber protein and penton or hexon protein adenovirus serotypes.

29. (withdrawn) The method according to claim 28, wherein said producing a library of chimeric viral particles comprises generating a library of chimeric capsids.

30. (withdrawn) The method according to claim 28, further comprising screening the produced chimeric viral particles for properties selected from the group consisting of target cell specificity, immunogenicity, re-directed neutralization, re-directed hemagglutination, infection efficiency, toxicity, and pharmacokinetics.

31. (withdrawn) The method according to claim 28, wherein said providing a nucleic acid library comprises providing a plurality of nucleic acids encoding proteins of like

functions for differing adenovirus serotypes, and wherein the plurality of nucleic acids encoding proteins of like functions for differing adenovirus serotypes are flanked by uniform restriction sites.

32. (withdrawn) A method for selecting a producing a chimeric adenovirus having a desired host range determined by at least one part of a fiber of a first adenovirus subtype, immunological properties determined by at least one part of at least one of a hexon or a penton of a second adenovirus serotype, said method comprising:

providing a recombinant vector derived from the genome of adenovirus serotype 5, said recombinant vector comprising at least on ITR and a packaging signal and having an insertion site for a gene of interest, said recombinant vector further having an insertion site for a nucleic acid encoding at least one part of a fiber protein of the first adenovirus serotype and having an insertion site for functionally inserting a nucleic acid encoding at least one part of at least one of a penton or a hexon protein of the second serotype of adenovirus;

providing a nucleic acid library comprising a plurality of nucleic acids encoding a plurality of adenoviral proteins of a plurality of adenovirus serotypes, at least some of said plurality of nucleic encoding proteins of like functions for differing adenovirus serotypes;

providing said plurality of nucleic acids flanked by restriction sites wherein said restriction sites correspond to said insertion sites in said recombinant vector and wherein the at least some

of the plurality of nucleic acids encoding proteins of like functions for differing adenovirus serotypes are flanked by uniform restriction sites;

inserting into said recombinant vector at least one first nucleic acid from said nucleic acid library, said at least one first nucleic acid obtained from the second adenovirus serotype and encoding at least on part of at least one of a penton or hexon protein, said penton or hexon protein having lower antigenicity relative to penton or hexon proteins of the first adenoviral serotype and resulting in a viral particle having lower antigenicity;

inserting into said recombinant vector at least one second nucleic acid from said nucleic acid library, said at least one second nucleic acid obtained from the first adenovirus serotype and encoding at least one function part of a fiber protein having the desired host range;

inserting said gene of interest into said recombinant vector;

providing at least one packaging cell;

transfecting said recombinant vector into said at least one packaging cell; and

producing chimeric viral particles.

33. (currently amended) A chimeric adenovirus comprising:

an adenoviral capsid ~~derived~~ from a first adenovirus serotype; and

a part of an adenoviral fiber ~~derived~~ from a second adenovirus serotype substituted for a corresponding part of a fiber of the capsid ~~derived~~ from the first adenovirus serotype, the second adenovirus serotype selected from the group consisting of serotypes 11, 14, 16,

21, 34, 35, and 50, wherein the part of the adenoviral fiber ~~derived~~ from the second adenovirus serotype is fused to a tail region of a fiber of the first adenovirus serotype.

34. (previously presented) The chimeric adenovirus of claim 33 wherein the first adenovirus serotype is serotype 5.

35. (currently amended) A chimeric adenovirus comprising:
an adenoviral capsid ~~derived~~ from a first adenovirus serotype; and
a part of an adenoviral fiber ~~derived~~ from adenovirus serotype 35 substituted for a corresponding part of a fiber of the capsid ~~derived~~ from the first adenovirus serotype, the part of the adenoviral fiber ~~derived~~ from adenovirus serotype 35 fused to a tail region of a fiber of the first adenovirus serotype.

36. (previously presented) The chimeric adenovirus of claim 35 wherein the first adenovirus serotype is serotype 5.

37. (currently amended) A method for producing a chimeric adenoviral particle having a capsid ~~derived~~ from a first adenovirus serotype exhibiting a desired tropism and antigenicity determined by a part of a fiber of a second adenovirus serotype, the second adenovirus serotype selected from the group consisting of serotypes 11, 14, 16, 21, 34, 35, and 50, the method comprising:

providing a recombinant vector ~~derived~~ from the first adenovirus serotype comprising at least one ITR, a packaging signal, an insertion site for a nucleic acid sequence of interest, and an insertion site for a gene sequence encoding a ~~functional~~ part of a fiber protein of the second adenovirus serotype;

inserting into the recombinant vector the gene sequence encoding the ~~functional~~ part of the fiber protein of the second adenovirus serotype, wherein the ~~functional~~ part of the fiber protein of the second adenovirus serotype is fused to a tail region of a fiber of the first adenovirus serotype;

transfecting said vector in a packaging cell; and

producing chimeric adenoviral particles.

38. (previously presented) The method according to claim 35 wherein the first adenovirus serotype is serotype 5.

39. (previously presented) The method according to claim 35 wherein the recombinant vector comprises a plasmid.

40. (currently amended) A method for producing a chimeric adenoviral particle having a capsid ~~derived~~ from a first adenovirus serotype exhibiting a desired tropism and antigenicity determined by a part of a fiber ~~derived~~ from adenovirus serotype 35, the method comprising:

~~the fiber protein of adenovirus serotype 35;~~

inserting into a vector a gene sequence encoding ~~the functional part~~ a shaft and knob region of

~~the a fiber protein derived~~ from adenovirus serotype 35, wherein the ~~functional part of the~~

~~fiber protein of the second adenovirus serotype~~ shaft and knob region is fused to a tail

region of a fiber of the first adenovirus serotype;

transfecting said vector in a packaging cell; and

producing chimeric viral particles.

41. (previously presented) The method according to claim 40 wherein the first adenovirus serotype is serotype 5.

42. (previously presented) The method according to claim 40 wherein the recombinant vector comprises a plasmid.

43. (currently amended) A recombinant vector ~~derived from~~ based on a first adenovirus serotype comprising:

- at least one ITR;
- a packaging signal;
- a first insertion site for a nucleic acid sequence of interest;
- a second insertion site for ~~functionally~~ inserting a gene sequence encoding a part of a fiber protein of a second adenovirus serotype, the second adenovirus serotype selected from the group consisting of serotypes 11, 14, 16, 21, 34, 35, and 50; and
- a gene sequence encoding the part of the fiber protein of the second adenovirus serotype inserted in the second insertion site, the part of the fiber protein of the second adenovirus serotype exhibiting a desired tropism to a plurality of cells in a host and fused to a tail region of a fiber of the first adenovirus serotype.

44. (previously presented) The recombinant vector of claim 43 wherein the recombinant vector comprises a plasmid.

45. (previously presented) The recombinant vector of claim 43 wherein the first adenovirus serotype is serotype 5.

46. (currently amended) A recombinant vector ~~derived from~~ based on a first adenovirus serotype comprising:

- at least one ITR;
- a packaging signal;
- a first insertion site for a nucleic acid sequence of interest;
- a second insertion site for ~~functionally~~ inserting a gene sequence encoding a part of a fiber protein of adenovirus serotype 35; and
- a gene sequence encoding the part of the fiber protein of adenovirus serotype 35 inserted in the second insertion site, the part of the fiber protein of adenovirus serotype 35 exhibiting a desired tropism to a plurality of cells in a host and fused to a tail region of a fiber of the first adenovirus serotype.

47. (previously presented) The recombinant vector of claim 46 wherein the recombinant vector comprises a plasmid.

48. (previously presented) The recombinant vector of claim 46 wherein the first adenovirus serotype is serotype 5.

49. (currently amended) An improved chimeric adenovirus of the type having a capsid ~~derived~~ from a first adenovirus serotype and a chimeric adenoviral fiber protein, wherein the improvement comprises:

said chimeric adenoviral fiber protein having a tail region of a fiber protein from said first adenovirus serotype operatively linked to a part of a fiber protein from adenovirus serotype 35.

50. (currently amended) An improved method for producing a chimeric adenoviral particle of the type having a capsid ~~derived~~ from a first adenovirus serotype and a fiber protein sequence derived in part from a second adenovirus serotype, the improvement comprising:
providing in said chimeric adenoviral particle a gene sequence encoding a tail region of a fiber protein from said first adenovirus serotype operatively linked to a part of a fiber protein from adenovirus serotype 35.

Attorney Docket No.: 2578-4123.2
Serial No. 09/348,354
Amendment of August 19, 2003
Reply to Office Action of March 26, 2003

IN THE DRAWINGS:

Please change Figure 7 as presented in the replacement sheets provided in Appendix A.

Please change Figure 10 as presented in the replacement sheets provided in Appendix B.

Entry of the replacement FIGS. 7 and 10 is respectfully requested.